PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

DAVIES, Jonathan M.
REDDIE & GROSE
16, Theobalds Road
London WC1X 8PL
GRANDE BRETAGNE

File at Cambridge
SYSTEM ✓
JMD ✓ 30 mths ✓ 5m
5.9.99
RI 0

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

	Date of mailing *(day/month/year)* 08.06.99
Applicant's or agent's file reference 39161/JMD	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB98/00727	05/03/1998	05/03/1997

Applicant
ADPROTECH PLC., UNIT 3, et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

CAMBRIDGE
DUE DATE 5/9/99
INITIALS MH

RECEIVED
18 JUN 1999
CAMBRIDGE

Name and mailing address of the IPEA/
LONDON
European Patent Office
D-80298 Munich
Tel. (+49-89) 2399-0 Tx: 523656 epmu d
Fax: (+49-89) 2399-4465

Authorized officer
Hingel, W
Tel.(+49-89) 2399-8717

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
39161/JMD		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB98/00727	05/03/1998	05/03/1997
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant ADPROTECH PLC., UNIT 3, et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29/09/1998	03.06.99
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. (+49-89) 2399-0 Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Stolz, B Telephone No. (+49-89) 2399 8416

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB98/00727

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-58	as originally filed			

Claims, No.:

1-6	as originally filed			
7-27	as received on	24/05/1999	with letter of	24/05/1999

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-27
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-27
Industrial applicability (IA)	Yes:	Claims	1-27
	No:	Claims	

2. Citations and explanations

see separate sheet

1. Reasoned statement

1.1. The application describes sCR1-derived polypeptides comprising one two four SCRs selected from SCR 1 to 4 of the LHR-A of CR1 and comprising at least SCR 3. These peptides are useful in the regulation of complement activation and in the therapy of diseases involving complement activation.

1.2. Novelty (Art. 33(2) PCT)

The molecules of claims 1 to 19 do not seem to have been described in the cited prior art. They and their uses are therefore novel.

1.3. Inventive step (Art. 33(3) PCT)

Truncated versions of CR1 suitable for the same purposes have been described in e.g. WO95/08343 (pp. 8/9), EP0512733 (pp. 5/6), and WO94/00571 (D1). D1 (by the same inventors) revealed a soluble polypeptide comprising one to four SCRs selected from SCR 1 to 4 from the LHR-A as the only structurally and functionally intact SCR domains and including at least SCR3 but did not comprise the presently claimed mutants.

In light of the cited prior art, the underlying technical problem can be identified as the provision of further polypeptides suitable as regulators of complement activation.

The presented solutions to this problem are the polypeptides of claims 1 to 18. These are basically the same polypeptides as in D1 except for the additional mutations as specified. D1 referred to the usefulness of mutations in general terms (p. 3, lines 2 to 7). WO95/08343 described a number of mutations in a different soluble CR1 fragment. Among others, mutations G79D (p. 38) and E116K (p. 35) were described. A number of mutations affecting residues 79 and 109 are also described in EP 0512733 (Tables 1 to 3). Since mutating the molecules of D1 had been suggested and some potentially uselful positions were already tested in a related polypetide, it appears that at least some of the claimed solutions to the above identified problem would have been obvious to the person

of skill. However, it is also noted that the applicants did not simply suggest to incorporate all the mutations described in the prior art, but made a selection. Such a selection can be inventive, provided it is associated with an unexpected technical effect. The same criterion applies to the newly identified mutants. In light of the cited prior art, it is not sufficient to merely suggest new mutants, but the additional mutants need to show an unexpected effect.

The only example tested seems to be the construct termed CM 7 (cf. p 41 of the description), which was found not to differ in its activity from the previously known molecule of D1. However, the applicant has informed the IPEA that more recent experimental data show a 50 to 75% percent increase in activity of the pseudogene construct. Thus, this partcular construct seems to be associated with an unexpected effect. At present it is not clear, if any of the other claimed mutants provide a similarly unexpected effect when compared to the unmutated molecules of D1. Adding a membrane anchoring sequence would seem to have been obvious in light of the disclosure of Coyne et al. (cited in the ISR). Since none of the claims seems to be specifically directed to only the construct termed CM 7 (comprising SCR1, SCR2 and mutated SCR3), all of claims 1 to 27 are considered to lack inventive step.

7. A polypeptide according to claim 6 wherein W^2, X^2, Y^2 and Z^2 represent residues 59-62, 121-124, 192-196, and residues 253 respectively, of mature CR1, optionally substituted as defined in claim 3, and V^2 represents residue 1 of mature CR1 optionally linked via its N-terminus to methionine.

8. A polypeptide according to claim 1 or 3 of formula (III):

$$NH_2\text{-}X^3\text{-}SCR3\text{-}Y^3\text{-}OH \qquad (III)$$

in which SCR3 is as hereinbefore defined, containing at least one of the substitutions as aforesaid, and in a preferred embodiment, all those of Sequence Group 1, and X^3 and Y^3 represent bonds or short linking sequences of amino acids, preferably 1 to 5 residues in length and which are preferably derived from native interdomain sequences in CR1, optionally substituted as defined in claim 3.

9. A polypeptide according to claim 8 wherein X^3 represents amino acids 122-124 of mature CR1, optionally substituted as defined in claim 3, optionally linked to methionine at its N-terminus and Y^4 represents amino acids 192-196 of mature CR1.

10. A polypeptide according to claim 1 or 3 of formula (IV):

$$NH_2\text{-}X^4\text{-}SCR3\text{-}Y^4\text{-}SCR4\text{-}Z^4\text{-}OH \qquad (IV)$$

in which SCR3 and SCR4 are as hereinbefore defined containing at least one of the substitutions as aforesaid and X^4, Y^4 and Z^4 represent bonds or short linking sequences of amino acids, preferably 1 to 5 residues in length and which are preferably derived from native interdomain sequences in CR1, optionally substituted as defined in claim 3.

11. A polypeptide according to claim 10 wherein X^4 represents amino acids 122-124 of mature CR1, optionally substituted as defined in claim 3, optionally linked to methionine at its N-terminus and Y^4 and Z^4 represent amino acids 192-196 and 253 respectively of mature CR1.

12. A polypeptide according to any preceding claim wherein the SCR3 domain is substituted with all ten residues found in the corresponding pseudogene sequence, namely (in single letter code):

A132, T137, I139, S140, Y143, H153, L156, R159, K161, K177 (Sequence Group 1)

and the remaining domains have the sequence of mature CRI.

13. A polypeptide according to claim 1 selected from SEQ ID NOs: 1, 9, 11, 13, 15, 17, , 19, 21, 23, 25, 27 and 29.

14. A soluble derivative of the soluble polypeptide of any preceding claim, said derivative comprising two or more heterologous membrane binding elements with low membrane affinity covalently associated with the polypeptide which elements are capable of interacting independently and with thermodynamic additivity with components of cellular membranes exposed to extracellular fluids.

15. A derivative according to claim 16 compring two to eight membrane binding elements selected from: fatty acid derivatives; ligands of known integral membrane proteins; sequences derived from the complementarity-determining region of monoclonal antibodies raised against epitopes of membrane proteins; membrane binding sequences identified through screening of random chemical libraries.

16. A derivative according to claim 14 or 15 having the following structure:

$[P]-\{L-[W]\}_n-X$

in which:

P is the soluble polypeptide,

each L is independently a flexible linker group,

each W is independently a peptidic membrane binding element,

n is an integer of 1 or more and

X is a peptidic or non-peptidic membrane-binding entity which may be covalently linked to any W.

17. A polypeptide derivative which is SEQ ID NO: 34, 49 or 51

18. The polypeptide portion of a derivative according to any of claims 14 to 17.

19. A polypeptide portion according to claim 18 which is SED ID NO: 31, 36, 50, 54 or 57

20.. A process for preparing a polypeptide according to any of claims 1 to 13 which process comprises expressing DNA encoding said polypeptide in a recombinant host cell and recovering the product.

21. A DNA polymer comprising a nucleotide sequence that encodes the polypeptide of any of claims 1 to 13, 18 or 19.

22 A DNA polymer according to claim 21 selected from SEQ ID NOs: 1,10, 12, 14, 16, 18, 20, 22, 24, 26, 28, or 30,

23. A replicable expression vector capable, in the host cell, of expressing the DNA polymer of claim 21 or 22

24. A host cell transformed with a replicable expression vector of claim 23.

25. A process for preparing a derivative according to any of claims 14 to 17 which process comprises expressing DNA encoding the polypeptide portion of said derivative in a recombinant host cell and recovering the product and thereafter post translationally modifying the polypeptide to chemically introduce membrane binding elements.

26. A pharmaceutical composition comprising a therapeutically effective amount of a polypeptide or derivative of any of claims 1 to17, and a pharmaceutically acceptable carrier or excipient.

27. A method of treating a disease or disorder associated with inflammation or inappropriate complement activation comprising administering to a subject in need of such treatment a therapeutically effective amount of a polypeptide or derivative of any of claims 1 to17.

28. The use of a polypeptide or derivative of any of claims 1 to17 in the manufacture of a medicament for the treatment of a disease or disorder associated with inflammation or inappropriate complement activation.

7. A polypeptide according to claim 6 wherein W^2, X^2, Y^2 and Z^2 represent residues 59-62, 121-124, 192-196, and residues 253 respectively, of mature CR1, optionally substituted as defined in claim 3, and V^2 represents residue 1 of mature CR1 optionally linked via its N-terminus to methionine.

8. A polypeptide according to claim 1 or 3 of formula (III):

$$NH_2\text{-}X^3\text{-SCR3-}Y^3\text{-OH} \qquad \text{(III)}$$

in which SCR3 is as hereinbefore defined, containing at least one of the substitutions as aforesaid, and in a preferred embodiment, all those of Sequence Group 1 aforesaid, and in a preferred embodiment, all those of Sequence Group 1, namely: A132, T137, I139, S140, Y143, H153, L156, R159, K161, K177, and X^3 and Y^3, and X^3 and Y^3 represent bonds or short linking sequences of amino acids, preferably 1 to 5 residues in length and which are preferably derived from native interdomain sequences in CR1, optionally substituted as defined in claim 3.

9. A polypeptide according to claim 8 wherein X^3 represents amino acids 122-124 of mature CR1, optionally substituted as defined in claim 3, optionally linked to methionine at its N-terminus and Y^4 represents amino acids 192-196 of mature CR1.

10. A polypeptide according to claim 1 or 3 of formula (IV):

$$NH_2\text{-}X^4\text{-SCR3-}Y^4\text{-SCR4-}Z^4\text{-OH} \qquad \text{(IV)}$$

in which SCR3 and SCR4 are as hereinbefore defined containing at least one of the substitutions as aforesaid and X^4, Y^4 and Z^4 represent bonds or short linking sequences of amino acids, preferably 1 to 5 residues in length and which are preferably derived from native interdomain sequences in CR1, optionally substituted as defined in claim 3.

11. A polypeptide according to claim 10 wherein X^4 represents amino acids 122-124 of mature CR1, optionally substituted as defined in claim 3, optionally linked to methionine at its N-terminus and Y^4 and Z^4 represent amino acids 192-196 and 253 respectively of mature CR1.

12. A polypeptide according to any preceding claim wherein the SCR3 domain is substituted with all ten residues found in the corresponding pseudogene sequence, namely (in single letter code):
A132, T137, I139, S140, Y143, H153, L156, R159, K161, K177 (Sequence Group 1)
and the remaining domains have the sequence of mature CRI.

13. A polypeptide according to claim 1 selected from SEQ ID NOs: 1, 9, 11, 13, 15, 17, , 19, 21, 23, 25, 27 and 29.

14. A soluble derivative of the soluble polypeptide of any preceding claim, said derivative comprising two or more heterologous membrane binding elements with low membrane affinity covalently associated with the polypeptide which elements are capable

of interacting independently and with thermodynamic additivity with components of cellular membranes exposed to extracellular fluids.

15. A derivative according to claim 14 compring two to eight membrane binding elements selected from: fatty acid derivatives; ligands of known integral membrane proteins; sequences derived from the complementarity-determining region of monoclonal antibodies raised against epitopes of membrane proteins; membrane binding sequences identified through screening of random chemical libraries.

16. A derivative according to claim 14 or 15 having the following structure:

$[P]-\{L-[W]\}_n-X$

in which:

P is the soluble polypeptide,

each **L** is independently a flexible linker group,

each **W** is independently a peptidic membrane binding element,

n is an integer of 1 or more and

X is a peptidic or non-peptidic membrane-binding entity which may be covalently linked to any **W**.

17. A polypeptide derivative which is SEQ ID NO: 34, 49 or 51

18. The polypeptide portion of a derivative according to any of claims 14 to 17, wherein the polypeptide portion is SEQ ID NO: 31, 36, 50, 54 or 57.

19. A process for preparing a polypeptide according to any of claims 1 to 13 which process comprises expressing DNA encoding said polypeptide in a recombinant host cell and recovering the product.

20. A DNA polymer comprising a nucleotide sequence that encodes the polypeptide of any of claims 1 to 13, or 18.

21. A DNA polymer according to claim 20 selected from SEQ ID NOs: 1,10, 12, 14, 16, 18, 20, 22, 24, 26, 28, or 30,

22. A replicable expression vector capable, in the host cell, of expressing the DNA polymer of claim 20 or 21.

23. A host cell transformed with a replicable expression vector of claim 22.

24. A process for preparing a derivative according to any of claims 14 to 17 which process comprises expressing DNA encoding the polypeptide portion of said derivative in a recombinant host cell and recovering the product and thereafter post translationally modifying the polypeptide to chemically introduce membrane binding elements.

25. A pharmaceutical composition comprising a therapeutically effective amount of a polypeptide or derivative of any of claims 1 to17, and a pharmaceutically acceptable carrier or excipient.

26. A method of treating a disease or disorder associated with inflammation or inappropriate complement activation comprising administering to a subject in need of such treatment a therapeutically effective amount of a polypeptide or derivative of any of claims 1 to17.

27. The use of a polypeptide or derivative of any of claims 1 to17 in the manufacture of a medicament for the treatment of a disease or disorder associated with inflammation or inappropriate complement activation.

AMENDED SHEET

GB

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
39161/JMD		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 98/ 00727	05/03/1998	05/03/1997
Applicant		
ADPROTECH PLC., UNIT 3, et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [X] **Certain claims were found unsearchable** (see Box I).

2. [ ] **Unity of invention is lacking** (see Box II).

3. [X] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing

   [X] filed with the international application.

   [ ] furnished by the applicant separately from the international application,

   [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

   [ ] Transcribed by this Authority

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant

   [X] the text has been established by this Authority to read as follows:

   COMPLEMENT RECEPTOR TYPE 1 (CR1)-LIKE SEQUENCES

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

   Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 98/00727

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim(s) 27 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 98/00727

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C12N1/21 C07K14/705 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 94 00571 A (SMITHKLINE BEECHAM PLC ;SMITH RICHARD ANTHONY GODWIN (GB); DODD IA) 6 January 1994 cited in the application see the whole document ---	1-11,13, 18-24, 26-28
Y	WO 95 08343 A (UNIV WASHINGTON) 30 March 1995 see the whole document ---	1-11, 13-28
Y	EP 0 512 733 A (UNIV WASHINGTON) 11 November 1992 cited in the application see the whole document --- -/--	1-11, 13-28

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 July 1998	12/08/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Smalt, R

2

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,Y	WO 98 02454 A (ADPROTECH PLC ;SMITH RICHARD ANTHONY GODWIN (GB); DODD IAN (GB); M) 22 January 1998 see the whole document	14-17,25
A	HOURKADE, D. ET AL.: "Duplication and divergence of the amino-terminal coding region of the complement receptor 1 (CR1) gene." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 265, no. 2, 15 January 1990, pages 974-980, XP002072410 cited in the application see the whole document	
A	MAKRIDES, S.C. ET AL.: "Cell surface expression of the C3b/C4b receptor (CR1) protects chinese hamster ovary cells from lysis by human complement." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 267, no. 34, 5 December 1992, pages 24754-61, XP002072411 cited in the application see the whole document	
A	COYNE K E ET AL: "MAPPING OF EPITOPES, GLYCOSYLATION SITES, AND COMPLEMENT REGULATORY DOMAINS IN HUMAN DECAY ACCELERATING FACTOR" JOURNAL OF IMMUNOLOGY, vol. 149, no. 9, 1 November 1992, pages 2906-2913, XP002025305 see figure 7	14-17,25

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 98/00727

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9400571 A	06-01-1994	EP 0649468 A	26-04-1995
		JP 7508516 T	21-09-1995
WO 9508343 A	30-03-1995	AU 691525 B	21-05-1998
		AU 7842494 A	10-04-1995
		CA 2171953 A	30-03-1995
		EP 0730469 A	11-09-1996
		JP 9506764 T	08-07-1997
EP 0512733 A	11-11-1992	AU 657751 B	23-03-1995
		AU 1590292 A	05-11-1992
		CA 2067653 A	04-11-1992
		JP 6016696 A	25-01-1994
		US 5545619 A	13-08-1996
		US 5719127 A	17-02-1998
WO 9802454 A	22-01-1998	AU 3693997 A	09-02-1998

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 23 October 1998 (23.10.98)	
International application No. PCT/GB98/00727	**Applicant's or agent's file reference** 39161/JMD
International filing date (day/month/year) 05 March 1998 (05.03.98)	**Priority date** (day/month/year) 05 March 1997 (05.03.97)
Applicant MOSSAKOWSKA, Danuta, Ewa, Irena et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

29 September 1998 (29.09.98)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b):

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Céline Faust
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992) 2300272

Copy f r the Elected Office (EO/US)

PATENT COOPERATION TI ATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

DAVIES, Jonathan, Mark
Reddie & Grose
16 Theobalds Road
London WC1X 8PL
ROYAUME-UNI

Date of mailing (day/month/year)
20 August 1999 (20.08.99)

IMPORTANT NOTIFICATION

Applicant's or agent's file reference
39161/JMD

International application No.
PCT/GB98/00727

International filing date (day/month/year)
05 March 1998 (05.03.98)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address
COX, Vivienne, Frances
AdProTech plc
Unit 3
2 Orchard Road
Royston
Herts SG8 5HD
United Kingdom

State of Nationality: GB
State of Residence: GB
Telephone No.:
Facsimile No.:
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address
COX, Vivienne, Frances
AdProTech plc
Second floor, Units 7 & 8
The Maltings, Green Drift
Royston
Herts SG8 5DY
United Kingdom

State of Nationality: GB
State of Residence: GB
Telephone No.:
Facsimile No.:
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
Céline Faust

Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994)

0028026

PATENT COOPERATION T. ATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

DAVIES, Jonathan, Mark
Reddie & Grose
16 Theobalds Road
London WC1X 8PL
ROYAUME-UNI

Date of mailing (day/month/year)	
20 August 1999 (20.08.99)	
Applicant's or agent's file reference	**IMPORTANT NOTIFICATION**
39161/JMD	
International application No.	**International filing date** (day/month/year)
PCT/GB98/00727	05 March 1998 (05.03.98)

1. The following indications appeared on record concerning:

[X] the applicant [ ] the inventor [ ] the agent [ ] the common representative

Name and Address

ADPROTECH PLC
Unit 3
2 Orchard Road
Royston
Herts SG8 5HD
United Kingdom

State of Nationality	State of Residence
GB	GB

Telephone No.

Facsimile No.

Teleprinter No.

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[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Céline Faust
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994) 002802671

PATENT COOPERATION T[illegible]ATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

DAVIES, Jonathan, Mark
Reddie & Grose
16 Theobalds Road
London WC1X 8PL
ROYAUME-UNI

Date of mailing (day/month/year)
20 August 1999 (20.08.99)

Applicant's or agent's file reference
39161/JMD

IMPORTANT NOTIFICATION

International application No.
PCT/GB98/00727

International filing date (day/month/year)
05 March 1998 (05.03.98)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address
SMITH, Richard, Antony, Godwin
AdProTech plc
Unit 3
2 Orchard Road
Royston
Herts SG8 5HD
United Kingdom

State of Nationality: GB
State of Residence: GB
Telephone No.:
Facsimile No.:
Teleprinter No.:

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Name and Address
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AdProTech plc
Second floor, Units 7 & 8
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Céline Faust

Telephone No.: (41-22) 338.83.38